CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75203

CORRESPONDENCE

ANDA 75-203

Watson Laboratories, Inc.
Attention: Ernest Lengle, Ph.D.
311 Bonnie Circle
P.O. Box 1900
Corona, CA 91780-1900

AUG 2 1999

Dear Sir:

This is in reference to your abbreviated new drug application dated September 11, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Propafenone Hydrochloride Tablets, 150 mg, 225 mg, and 300 mg.

Reference is also made to your amendments dated April 29, October 16, December 28, 1998; and March 16, June 17, and July 16, 1999.

This application is deficient and, therefore, not approvable under 21 CFR 314.125(b)(13) because the Center for Drug Evaluation and Research (CDER) is unable to find that the methods used in, and the facilities and controls used for, the manufacture, processing, packaging or holding of your drug product, by Watson Laboratories, Inc., comply with current good manufacturing practice (CGMP) regulations.

Our conclusion is based upon the findings revealed during an inspection of Watson Laboratories, Inc.'s Corona, CA, manufacturing facility by representatives of the United States Food and Drug Administration from January 26, 1999, through March 12, 1999. Upon review of the inspectors' report and observations, we have received a recommendation from our Division of Manufacturing and Product Quality (DMPQ), Office of Compliance, to withhold approval of your abbreviated application.

Until such time as it can be demonstrated to the Agency that the CGMP-related issues associated with your Corona, CA manufacturing facility have been corrected and the Agency's concerns are otherwise satisfied, your application cannot be approved.

You should amend this application when your have been informed by a representative of the Office of Compliance that the CGMP-related issues have been satisfactorily resolved. Your amendment submitted in response to this not approvable letter will be

considered as a MINOR AMENDMENT provided that the amendment contains no significant additional information necessary to remedy the CGMP deficiencies or to address concerns identified by the investigators. If, as a result of follow-up inspections related to the ongoing evaluation of this or other applications, it is necessary for you to significantly revise your procedures, controls or practices to correct the deficiencies, then the amendment will be considered to represent a MAJOR AMENDMENT.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 7/29/99

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-203

Watson Laboratories, Inc.
Attention: David C. Hsia, Ph.D.
311 Bonnie Circle
Corona CA 91720

OCT 17 1997

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated September 26, 1997 and the correspondence dated September 29, 1997.

NAME OF DRUG: Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg

DATE OF APPLICATION: September 11, 1997

DATE OF RECEIPT: September 15, 1997

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Sheila O'Keefe
Project Manager
(301) 827-5848

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-203
DUP/Jacket
Division File
Field Copy
HFD-600/Reading File
HFD-610/J.Phillips
HFD-92
HFD-615/M.Bennett
HFD-324/M.Lynch

Endorsement: HFD-615/PRickman, Chief, RSB /S/ date 10/14/97
HFD-615, GDavis, CSO /S/ 10/1/97 date
HFD-625, ~~MSmola~~, Sup. Chem. _____ date
WP File x:\new\firmsnz\watson\ltrs&rev\75203.ack
FT/njg/10/01/97
ANDA Acknowledgment Letter!

ARCHIVAL COPY

WATSON Laboratories, Inc.

A Subsidiary of Watson Pharmaceuticals, Inc.

NDA ORIG AMENDMENT
PPL
AC

October 16, 1998

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Major Amendment

RE: **ANDA 75-203**
Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg

INCLUDING FINAL PRINTED LABELINGS

Dear Mr. Sporn:

Pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act and 21 CFR §314.96, Watson Laboratories Inc. is submitting this amendment to provide a complete response to the comments included in the FDA letter dated August 26, 1998 (copy attached) pertaining to the referenced ANDA.

We have enclosed one (1) archival, one (1) review, and in accordance with 21 CFR § 314.94(5), one (1) field copy of the application will be forwarded to the LA District Office.

Watson Laboratories, Inc. certifies that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application.

We trust the information submitted is sufficient for this amendment to be evaluated. Please contact me by phone at (909) 270-1400 or by fax at (909) 270-1428 if you have any questions or if I can assist you with the review of this application.

Sincerely,

RECEIVED
OCT 20 1998
GENERIC DRUGS

Ron Lapré
Senior Director, Regulatory Affairs

311 Bonnie Circle, PO Box 1900 Corona, California 91718-1900 • Tel: 909/270-1400 • Fax: 909/270-1096

WATSON
Laboratories, Inc.
A Subsidiary of Watson Pharmaceuticals, Inc.

October 16, 1998

Ms. Elaine C. Messa
District Director
Food & Drug Administration
19900 MacArthur Blvd., Suite 300
Irvine, California 92715

Major Amendment

RE: **Field Copy**
ANDA 75-203
Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg

Dear Ms. Messa:

Pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act and 21 CFR §314.96, Watson Laboratories, Inc. has submitted an amendment to the referenced ANDA to the Office of Generic Drugs. In accordance with 21 CFR §314.94(5), Watson is providing the enclosed Field Copy (1 volume) of the application to the LA District Office.

Watson Laboratories, Inc. certifies that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application.

Should you require additional information, please contact me at (909) 270-1400.

Sincerely,

Ron Lapré
Senior Director,
Regulatory Affairs

311 Bonnie Circle, PO Box 1900 Corona, California 91718-1900 • Tel: 909/270-1400 • Fax: 909/270-1096

ARCHIVAL
COPY

WATSON
Laboratories, Inc.
A Subsidiary of Watson Pharmaceuticals, Inc.

NDA ORIG AMENDMENT
FA

July 16, 1999

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

TELEPHONE AMENDMENT

RE: **ANDA 75-203**
Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg

Dear Mr. Sporn:

In a letter dated July 16, 1999, OGD requested that Watson Laboratories, Inc. amend ANDA 75-203 (Propafenone Hydrochloride Tablets) to include an exclusivity statement regarding a new indication (I-209) for the reference listed drug, Rythmol®. In compliance with this request, please find enclosed one (1) archival and one (1) review copy of Watson's Exclusivity Statement for the new indication.

In accordance with 21 CFR §314.94(d)(5), one (1) field copy of this amendment will be forwarded to the LA District Office. Watson Laboratories, Inc. certifies that the Field Copy is a true copy of the amendment submitted to OGD.

We believed that we have resolved all questions/concerns expressed by FDA in the above mentioned letter. If you have any questions or if I can assist you with the review of this application, please contact me by phone at (909) 270-1400 or by fax at (909) 278-0967.

Sincerely,

Ernest Lengle, Ph.D.
Senior Director, Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUL 22 1999
OGD

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4.1

WATSON
Laboratories, Inc.

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Subsidiary of Watson Pharmaceuticals, Inc.

Labeling Review
drafted 6/29/99
C. Vega

June 16, 1999

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

FACSIMILE AMENDMENT

NEW CORRESP
NC to Fax

RE: **ANDA 75-203**
Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg

INCLUDING FINAL PRINTED LABELING

Dear Mr. Sporn:

Pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act and 21 CFR §314.96, Watson Laboratories Inc. is submitting this amendment to provide a complete response to the comments included in the FDA letter dated May 18, 1999 (copy attached) pertaining to the referenced ANDA.

We have enclosed one (1) archival, one (1) review copy of the application (one volume each).

We trust the information submitted is sufficient for this amendment to be evaluated. Please contact me by phone at (909) 270-1400 or by fax at (909) 278-0967 if you have any questions or if I can assist you with the review of this application.

Sincerely,

Ernest Lengle, Ph.D.

Ernest E. Lengle, Ph.D.
Senior Director, Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUN 18 1999
OGD

le, PO Box 1900 Corona, California 91718-1900 • Tel: 909/270-1400 • Fax: 909/270-1096

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ARCHIVAL CO.

WATSON
Laboratories, Inc.
A Subsidiary of Watson Pharmaceuticals, Inc.

March 14, 2000

ORIG AMENDMENT
N/AA

Mr. Gary Buehler
Acting Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place
Rockville, MD 20855

Re: Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg
ANDA 75-203

Dear Mr. Buehler:

In a March 2, 2000 conference call with OGD, Watson Laboratories, Inc. was informed that there were bioequivalence issues regarding Watson's Propafenone HCl Tablet Application (ANDA 75-203). Per OGD's request, Watson Laboratories, Inc. is withdrawing the 300 mg dosage strength wavier without prejudice to refiling at a later date. Watson is requesting, however, that this ANDA be approved for 150 mg and 225 mg strengths.

We believe that all questions and/or concerns expressed by FDA in the telephone call have been resolved. If you have any additional questions, please contact me by phone at (909) 270-1400 or by fax at (909) 278-0967.

Sincerely,

Ernest Lengle, Ph.D.

Ernest Lengle, Ph.D.
Sr. Director
Regulatory Affairs

CENTER FOR DRUG
RECD
MAR 15 2000
OGD
EVALUATION AND RESEARCH

311 Bonnie Circle, P.O. Box 1900, Corona, California 92878-1900 • Tel: 909/270-1400 • Fax: 9

ARCHIVAL COPY

NAE mDA 6/30/98

WATSON Laboratories, Inc.

A Subsidiary of Watson Pharmaceuticals, Inc.

June 15, 1998

NEW CORRESP NC

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Correspondence

RE: **ANDA 75-203**
Propafenone Hydrochloride Tablets, 150 mg, 225 mg, 300 mg
Abbreviated New Drug Application

Dear Mr. Sporn:

The referenced application was submitted by Watson Laboratories, Inc. on September 11, 1997. On October 17, 1997, OGD acknowledged receipt of the ANDA effective September 15, 1997. During the subsequent review cycle, we were informed by OGD that the application had been transferred to another review branch within the Division of Chemistry II. Based on our calculations, as of today this application has been at the OGD for 273 days.

We would greatly appreciate any information as to the status of the CMC review for this ANDA and any outstanding requirements that need to be fulfilled by Watson to expedite the review and approval process. I can be reached by telephone at (909) 270-1400, ext. 4141, or by fax at (909) 270-1428.

Sincerely yours,

I Spoke c Ron Lapre on 6/30/98 I informed him clam review was completed and is under going secondary review at the Division level. Told him I expected comm would be releasable by mid July

RECEIVED
JUN 16 1998
GENERIC DRUGS

Ron Lapré
Senior Director
Regulatory Affairs

RL/me

311 Bonnie Circle, PO Box 1900 Corona, California 91718-1900 • Tel: 909/270-1400 • Fax: 909/270-1096

ARCHIVAL
COPY

WATSON
Laboratories, Inc.

A Subsidiary of Watson Pharmaceuticals, Inc.

April 29,1998

ORIG AMENDMENT
N/AB

Dr. Dale P. Conner, Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Bioequivalency Amendment

RE: **ANDA 75-203**
Abbreviated New Drug Application
Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg

Dear Dr. Conner:

Pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.96, Watson Laboratories is submitting this amendment to provide a complete response to the comments included in the FDA letter dated March 13, 1998 (copy attached) pertaining to the referenced ANDA. Our responses are given in the order in which the comments appear in the letter.

We have enclosed one (1) archival and one (1) review copy of this amendment.

We trust this information is sufficient for this amendment to be evaluated. If I can assist with the review of this application, please contact me by phone at (909) 270-1400 or by fax at (909) 270-1428.

Sincerely,

Ron Lapré
Senior Director
Regulatory Affairs

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APR 30 1998
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311 Bonnie Circle, PO Box 1900 Corona, California 91718-1900 • Tel: 909/270-1400 • Fax: 909/270-1096

WATSON
Laboratories, Inc.
Subsidiary of Watson Pharmaceuticals, Inc.

September 26, 1997

Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

BIOAVAILABILITY

Attention: Mr. Greg Davis

RE: Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg
ANDA #75-203

Dear Mr. Davis:

Pursuant to your telephone conversation on September 26, 1997, regarding to the above-referenced product, appended is the requested information:

> Corrected FDA Form 356h. (p.1), with the reference drug "RYTHMOL®" added;
> Corrected Request for *in vivo* bioequivalence waiver, showing the correct 225 mg strength (p.371).

We have provided one (1) archival copy and two (2) review copies.

We apologize for the oversight and extend our thanks for the telephone contact.

Please feel free to contact me at (909) 270-1400, or fax me at (909) 270-1428, if you have any questions or require additional information.

Sincerely,

Ron Lapré
Senior Director, Regulatory Affairs

RL/mc
enc

WATSON
Laboratories, Inc.

A Subsidiary of Watson Pharmaceuticals, Inc.

labeling review completed. Hodgman 11/3/97

505(j)(ii) q OK 10/1/97 Gregory S. Davis

September 11, 1997

Mr. Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food & Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RECEIVED
SEP 15 1997

RE: **Abbreviated New Drug Application**
Propafenone Hydrochloride Tablets, 150 mg, 225 mg, and 300 mg

Dear Mr. Sporn:

Pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act and 21 CFR §314.92, Watson Laboratories Inc. submits herein an original Abbreviated New Drug Application for Propafenone Hydrochloride Tablets, 150 mg, 225 mg and 300 mg.

The drug product described above is the same as RYTHMOL®, from Knoll Laboratories. We have submitted comparative information to indicate that our product is the same as the reference listed drug product. This information is presented in tabular form, comparing active ingredient, conditions of use, route of administration, dosage form, strength, bioequivalence, and labeling for the products as supplied by Watson Laboratories, Inc. and by Knoll Laboratories.

We have enclosed one (1) archival, one (1) review, and in accordance with 21 CFR § 314.94(5), one (1) field copy of the application will be forwarded to the LA District Office.

Watson Laboratories, Inc. certifies that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application.

As required, three (3) additional separately bound copies of the analytical methods and descriptive information needed to perform the tests on the samples (both the bulk active ingredient and finished dosage form) are included as one of the volumes of the archival copy of this ANDA.

Cont'd/....2

311 Bonnie Circle, Corona, California 91720 • Tel: 909/270-1400 • Fax: 909/270-1096

The number of volumes in the archival, review, and field copies of the ANDA are as follows:

Blue Archival Copy	- 17 volumes
Orange Review Copy	- 15 volumes
Red Review Copy	- 2 volumes
Burgundy Field Copy	- 2 volumes

In addition, for the Bioequivalence Section, we have also enclosed computer diskettes with the analytical data and bioavailability parameters in the format prescribed by the FDA. These diskettes are located at the front of Section VI of the Orange Review Copy of this application.

We trust the information submitted is sufficient for this Abbreviated New Drug Application to be evaluated. Please contact me by phone at (909) 270-1400 or by fax at (909) 270-1428 if you have any questions or if I can assist you with the review of this application.

Sincerely,

David C. Hsia, Ph.D.
Executive V.P., Research & Development
WATSON LABORATORIES, INC.